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Novel base-pairing interactions at the tRNA wobble position crucial for accurate reading of the genetic code

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Abstract

Posttranscriptional modifications at the wobble position of transfer RNAs play a substantial role in deciphering the degenerate genetic code on the ribosome. The number and variety of modifications suggest different mechanisms of action during messenger RNA decoding, of which only a few were described so far. Here, on the basis of several 70S ribosome complex X-ray structures, we demonstrate how Escherichia coli tRNA Lys UUU with hypermodified 5-methylaminomethyl-2-thiouridine (mnm 5 s 2 U) at the wobble position discriminates between cognate codons AAA and AAG, and near-cognate stop codon UAA or isoleucine codon AUA, with which it forms pyrimidine-pyrimidine mismatches. We show that mnm 5 s 2 U forms an unusual pair with guanosine at the wobble position that expands general knowledge on the degeneracy of the genetic code and specifies a powerful role of tRNA modifications in translation. Our models consolidate the translational fidelity mechanism proposed previously where the steric complementarity and shape acceptance dominate the decoding mechanism.

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